Mitchell's Miracles explains the TREATMENT FOR NEUROBLASTOMA

Once it has been confirmed that a child has neuroblastoma and the disease has been staged, there will be a distinct treatment plan which aims to reduce the size of the primary tumour with chemotherapy, so that removal of all **or** most of the tumour is possible with surgery, with the aim to achieve remission and to ensure the Neuroblastoma cancer does not return.

The treatment will be different for each stage of this disease. But here, we will discuss the 'frontline' protocol ahead for those children/teenagers who are diagnosed as 'high-risk', stage 4 neuroblastoma.

Before a child is diagnosed with Neuroblastoma, the doctors will run various tests based on symptoms.

- **Blood tests**
- **Urine test to check the VMA** - Urine tests look for hormones that are released by neuroblastoma cells **Vanillylmandelic acid** (VMA) and other catecholamine metabolites such as homovanillic acid (HVA) measurement in urine are used for screening children for catecholamine-secreting tumors such as neuroblastoma and other neural crest tumors and monitoring those who have had treatment for these tumors.

  More than 90% of individuals with neuroblastoma have elevated VMA and/or HVA.

  What is the normal range of VMA?
  Normal Values:

  VMA: **2 to 7 mg/24-hours**.

- **Imaging** to stage the cancer will include X-rays, bone scans, CT, MRI and MIBG scans

MYCN / MYC gene explained.

When a diagnosis of Neuroblastoma is confirmed, a bone marrow aspiration and samples of the primary tumour (after removal) will analyze the gene to determine whether it is MYCN or MYC.

Gene amplification of MYCN was one of the earliest genetic markers discovered in neuroblastoma and is still one of the strongest predictors of poor prognosis. The prevalence of MYCN amplification in neuroblastoma patients is **20%–30%** and the overall survival for these patients remains at less than 50% (23–25).

MYCN is an ***oncogene***,a **gene** that helps control cell growth. Neuroblastoma tumors that have too many copies of MYCN tend to grow faster and may be harder to treat. Oncologists commonly call this ***MYCN-amplified.***

The start of Neuroblastoma treatment - unless it has been altered for the specific child due to other complications.

1. **Operation** to insert a **hickman line / Port** this is carried out under GA (General Anesthetic) this will be the line to take bloods, and receive medicines and blood products.
2. **Rapid Cojac** This is a combination of five chemotherapy's. (**cisplatin, vincristine, carboplatin, etoposide and cyclophosphamide**) that is delivered directly into your child's bloodstream through their central line. This therapy is administered in eight cycles, separated by intervals of ten days and is completed within 70 days of the first treatment. Modified N7 uses the drugs cyclophosphamide, doxorubicin, vincristine, cisplatin and etoposide.

One cycle lasts three-four days every three weeks, and there are five cycles. The child will also be given a 'growth factor' known as **G-CSF** as an injection, given daily between cycles to reduce the risk of infection In high-risk patients, the use of Rapid COJEC is to give high doses of chemotherapy over a shorter time which may improve survival.

3. **Why G-CSF is given and the Definition of febrile neutropenia explained** Febrile neutropenia is defined as having a neutrophil count of less than 1.0 x109/L **and** a temperature of 38°C or above on one occasion. Low temperatures < 36.0C may also indicate sepsis and the same guidelines should be followed as for febrile neutropenia. Any unwell child or young person who is receiving chemotherapy or radiotherapy should be considered at risk of infection even if afebrile and not neutropenic.

4. **Storing Cell's** During this induction chemotherapy, the child will have some of their 'peripheral haematopoietic stem cells' taken from their blood. These are cells that can develop into any of the different types of blood cells and so are very important for carrying oxygen, fighting infection, and preventing bleeding. During chemotherapy, these cells can get damaged and this can limit the amount of therapy your child can have as it takes some time for the blood to recover and for blood counts to improve. Taking some cells while they are healthy (**known as stem cell harvest**) and storing them during the induction phase means that these cells can be replaced later, therefore improving your child's ability to make new blood cells.
5. **Surgery** At this point, the tumour will have reduced in size since receiving Rapid Cojac chemotherapy so that the surgery will be as successful as it can be. However, if this isn't the case then the doctors will discuss other options.

The surgeon will remove the tumour along with a margin of healthy cells while trying to cause little disruption to the surrounding structures and organs.

The tumour that has been removed is then sent for further testing in the laboratory. This can provide a clearer picture of the genetic makeup **MYCN** or **MYC** (as mentioned above) of that tumour as well as identifying how much or how little of the tumour remains as active tissue.

Following surgery, a child with high-risk neuroblastoma will have high-dose chemotherapy to try and mop-up any remaining cancer cells.

6. **High Dose Chemotherapy** Known as consolidation therapy, high-dose chemotherapy aims to ‘mop-up’ any remaining cancer cells that might be left over following induction chemotherapy and surgery. This chemotherapy is known as 'myeloablative' and is high-dose. The term 'myeloablative' refers to the depletion of the blood-producing cells in the bone marrow as a side-effect. The drugs used in this process are called busulfan and melphalan.
7. **Side Effects** High-dose chemotherapy can have severe life-threatening toxicities, occurring in 4% of patients. Because the treatment requires several weeks in isolation while blood counts recover, the child is at risk of infection, and usually suffers from mouth sores and mucositis throughout the gastrointestinal tract. Children receive antibiotics, antifungal medications, and pain relief when needed, as well as blood products. Often they are on nutritional support due to the inability to eat, and this may require a feeding tube known as an NG tube, or in some cases due to mucositis throughout the gastrointestinal tract, a drip is given intravenously. Other adverse events include general condition, infection, stomatitis and **VOD** Veno-occlusive disease, which is also called sinusoidal obstruction syndrome (SOS), this happens when the small blood vessels that lead into the liver and are inside the liver become blocked. VOD is caused by high doses of chemotherapy and radiation therapy. **The drug (defibrotide Prociclide)** may be used to prevent or treat VOD. Most children

have mild to moderate VOD after high dose chemotherapy.and some will recover without treatment within a few weeks or after they get more of the drugs given to suppress the immune system. Sometimes VOD is severe and can lead to liver failure.

8. **Stem cell rescue** Giving higher doses of chemotherapy might be more effective in treating neuroblastoma but it causes severe damage to the bone marrow (where new blood cells are made). Doctors help children by replacing the bone marrow cells - this is called a stem cell transplant. These are the cells that were removed at the induction stage, and then harvested.

   The parents/carers are normally advised to drink a 1Ltr of water and have paracetamol at hand due to the strong smell of sweetcorn as it can cause headaches.

9. **Isolation** The child will be kept in isolation until they are no longer at risk of infection. They are at a high risk of infection because of their low white blood cell count. To help lower the risk of infection, your child will stay in a special hospital room and care is taken when family members visit.

10. **Immunotherapy** The aim of immunotherapy - also commonly referred to as antibody therapy - (as with any maintenance therapy) is to keep your child in remission and keep the cancer away.
    It helps the body's own defenses to turn against the neuroblastoma cells using antibodies.

    This should hopefully stop the cancer from returning as the body will learn to recognise and kill the cells. Immunotherapy is given into the bloodstream and is given every month for six months.

11. **Anti-GD2** The antibody used for neuroblastoma is called anti-GD2 and researchers had been testing a type called dinutuximab beta. GD2 is the substance found on the surface of many neuroblastoma cells.

    Towards the end of frontline treatment, some families may plan to look towards clinical trials which could be happening in other

Countries. But before doing this, please consult with your child's doctor.

Mitchell's Miracles are affiliated with a few amazing charities, and like us, have the best knowledge and understanding for Neuroblastoma cancer. If a clinical trial is an area you want to discuss, please contact '**Solving Kids' Cancer Charity.** They work alongside a range of other charities to push for the outcome of NICE recommending the life-saving drug for NHS use in England and Wales.

If you need any more information, please contact support@mitchellsmiracles.co.uk